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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.
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09/492,971 01/27/00 VOGEL

T 25775-C JFW/

EXAMINER
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HM19/1106

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MITRA.R	
ART UNIT	PAPER NUMBER

1653

DATE MAILED:

11/06/01

Please find below and/or attached an Office communication concerning this application or proceeding.

Commissioner of Patents and Trademarks

<b>Office Action Summary</b>	Application No.		Applicant(s)	
	09/492,971		VOQEL ET AL.	
	Examiner		Art Unit	
	Rita Mitra		1653	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

#### Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136 (a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If the period for reply specified above is less than thirty (30) days, a reply within the statutory minimum of thirty (30) days will be considered timely.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133).
- Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

#### Status

- 1) ☒ Responsive to communication(s) filed on 17 August 2001.
- 2a) ☐ This action is **FINAL**.                      2b) ☒ This action is non-final.
- 3) ☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

#### Disposition of Claims

- 4) ☒ Claim(s) 88-96 is/are pending in the application.
- 4a) Of the above claim(s) \_\_\_\_\_ is/are withdrawn from consideration.
- 5) ☐ Claim(s) \_\_\_\_\_ is/are allowed.
- 6) ☒ Claim(s) 88-96 is/are rejected.
- 7) ☐ Claim(s) \_\_\_\_\_ is/are objected to.
- 8) ☐ Claims \_\_\_\_\_ are subject to restriction and/or election requirement.

#### Application Papers

- 9) ☐ The specification is objected to by the Examiner.
- 10) ☐ The drawing(s) filed on \_\_\_\_\_ is/are objected to by the Examiner.
- 11) ☐ The proposed drawing correction filed on \_\_\_\_\_ is: a) ☐ approved b) ☐ disapproved.
- 12) ☐ The oath or declaration is objected to by the Examiner.

#### Priority under 35 U.S.C. § 119

- 13) ☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).
- a) ☐ All b) ☐ Some \* c) ☐ None of:
1. ☐ Certified copies of the priority documents have been received.
  2. ☐ Certified copies of the priority documents have been received in Application No. \_\_\_\_\_.
  3. ☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).
- \* See the attached detailed Office action for a list of the certified copies not received.
- 14) ☐ Acknowledgement is made of a claim for domestic priority under 35 U.S.C. § 119(e).

#### Attachment(s)

- |   |  |
|---|--|
| 15) <input type="checkbox"/> Notice of References Cited (PTO-892)                             | 18) <input type="checkbox"/> Interview Summary (PTO-413) Paper No(s). _____  |
| 16) <input type="checkbox"/> Notice of Draftsperson's Patent Drawing Review (PTO-948)         | 19) <input type="checkbox"/> Notice of Informal Patent Application (PTO-152) |
| 17) <input type="checkbox"/> Information Disclosure Statement(s) (PTO-1449) Paper No(s) _____ | 20) <input type="checkbox"/> Other: _____                                    |

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Art Unit: 1653

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### **DETAILED ACTION**

The Group and/or Art Unit location of your application in the PTO has changed. To aid in correlating any papers for this application, all further correspondence regarding this application should be directed to Group Art Unit 1653.

#### ***Status of the Claims***

Applicants' response to office action dated February 14, 2001 in paper #6, filed on August 17, 2001 is acknowledged. Claim 88 has been amended and entered. Therefore, claims 88-96 are currently pending and are under examination.

#### ***Terminal Disclaimer***

The terminal disclaimer filed on August 17, 2001 (paper #7), disclaiming the terminal portion of any patent granted on this application, which would extend beyond the expiration date of US Patent NOs. 5,270,030; 5,965,383 and 6,121,426 has been reviewed and is accepted. The terminal disclaimer has been recorded.

#### ***Response to Remarks and Arguments***

#### **Withdrawal of Rejections**

The rejection of claim 88 under **35 U.S.C. § 112, second paragraph** is withdrawn in view of applicants' amendment to claim 88 by deleting the word "capable".

The **obviousness-type double patenting** rejection is withdrawn in view of applicants' submitting a terminal disclaimer with respect to US 5270030, US 5965383 and US 6121426.

### **Maintenance of Rejections**

#### **Rejection under 35 U.S.C. 112, First Paragraph**

The following is a quotation of the first paragraph of 35 U.S.C. 112:

The specification shall contain a written description of the invention, and of the manner and process of making and using it, in such full, clear, concise, and exact terms as to enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the same and shall set forth the best mode contemplated by the inventor of carrying out his invention.

Claims 88-96 remain/are rejected under **35 U.S.C. 112, first paragraph**, because the specification, while being enabling for the fibronectin fragments disclosed in the specification, does not reasonably provide enablement for all portions of fibronectin. The specification does not enable a person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the invention commensurate in scope with these claims.

Claims 88-96 are directed to an imaging agent which comprises a polypeptide labeled with an imageable marker, wherein such polypeptide has an amino acid sequence which comprises at least one fifth of the amino acid sequence of the N-terminal fibrin binding domain of naturally-occurring fibronectin, wherein the imaging agent is capable of binding to fibrin. The claims are further directed to specific markers including radioactive isotopes, element opaque to x-rays and paramagnetic ions. The specification on page 53 describes three purified polypeptides, having molecular weights of 31 kD, 20 kD and 12 kD derived from the first 262 amino acids of the N-terminal sequence of fibrin binding domain of fibronectin. However, the specification does not define the one-fifth portion of the N-terminal sequence or any correlation between the one-fifth portion of sequence with the sequences from where the 31 kD, 20 kD and 12 kD polypeptides are derived.

Applicants' arguments and remarks on page 6-7 have been fully considered but not found persuasive. Specification page 47, lines 10-15 defined the 31 kD polypeptide as corresponding to an amino acid sequence present in the fibrin binding domain (FBD) and having the amino acid sequence 1-262 (Fig 1) of full length FBD of human fibronectin, further at page 11, lines 14-19 the specification indicates that FBD commences at amino acid position 1 of mature fibronectin, which is glutamine and corresponds to the fourth amino acid (Q) shown in Fig 1a, i.e. the N-terminus of FBD sequence is QAQQ. If FBD is commencing at amino acid position 1, it cannot lead to a conclusion that the N-terminus of FBD sequence is QAQQ. Furthermore applicants argue that one of ordinary skill in the art would be able to readily calculate the one fifth of 262 amino acids corresponds to about 52 amino acids, however neither the specification nor the claim defines clearly the position of this one fifth portion in relation to the amino acid sequence of the FBD of naturally occurring fibronectin. Applicants remark on page 7, lines 3-19 is solely based on an extrapolation of the description at pages 11 and 47 of the specification and further linking with the limitation of amended claim 88. However, one of skill in the art would not have the same interpretation and would have required undue experimentation for one of skill in the art to determine all possible imaging agents derivable, having at least one fifth of the amino acid sequence of the N-terminal region from the fibrin binding domain of fibronectin. A large number of such polypeptides are easily envisioned but the determination of the biological activity of all such polypeptides would require undue experimentation because the purification, refolding and labeling of all such polypeptides is well outside the realm of routine experimental work. One of skill would require guidance, lacking in the specification, as to exactly what polypeptides might possess the claimed activity. One of skill would require guidance as to what region of fibronectin is included in the phrase the "fibrin binding domain", what specific amino acids does this encompass, and what is the sequence. It is *a priori* unknown and unpredictable as to which of the large number of polypeptides encompassed by the scope of these claims would have the claimed biological activity i.e. being capable of binding to fibrin. The mere fact that a polypeptide derived from or a fragment of a domain having fibrin binding activity not necessarily would also have fibrin binding activity. Therefore, one of skill would require guidance in order to make and use of the claimed polypeptides, without such guidance the experimentation left to those skilled in the art is undue.

**Rejection under 35 U.S.C. 112, Second Paragraph**

The following is a quotation of the second paragraph of 35 U.S.C. 112:

“The specification shall conclude with one or more claims particularly pointing out and distinctly claiming the subject matter which the applicant regards as his invention.”

Claims 88-96 remain/are rejected under **35 U.S.C. 112, second paragraph**, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention.

It is not clear from the amended claim 88 or the specification that what is the corresponding amino acid sequence, which comprises at least one-fifth portion of the amino acid sequence of the N-terminal region of the fibrin binding domain of fibronectin. Furthermore, claim recites “...wherein the polypeptide has the amino acid sequence gln-ala-gln-gln or met-gln-ala-gln-gln at the N-terminus of the polypeptide”. This renders the claim indefinite because it is not clear what is the one-fifth portion of the amino acids in relation to the recited sequences, are these the one-fifth or is it one-fifth of these sequences? The amino acid sequences have not been given a sequence identifier, which makes the claim indefinite as to which sequences are defined in the claims. In addition claim 89 has a step of detecting but it is not clear from the claim that “detecting” would per se result in “imaging”. See for example, combining claim 89 and 96.

***Conclusion***

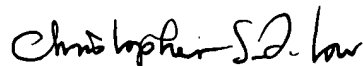
No claims are allowed.

*Inquiries*

Any inquiry concerning this communication or earlier communications from the Examiner should be directed to Rita Mitra whose telephone number is (703) 605-1211. The Examiner can normally be reached from 9:30 a.m. to 6:30 p.m. on weekdays. If attempts to reach the Examiner by telephone are unsuccessful, the Examiner's supervisor, Dr. Christopher Low, can be reached at (703) 308-2923. Papers related to this application may be submitted to Technology Center 1600 by facsimile transmission. Papers should be faxed to Technology Center 1600 via the PTO Fax Center located in Crystal Mall 1. The faxing of such papers must conform with the notice published in the Official Gazette, 1096 OG 30 (November 15, 1989). The Fax Center number is (703) 308-4242. Any inquiry of a general nature or relating to the status of this application should be directed to the Group receptionist whose telephone number is (703) 308-0196.



Rita Mitra, Ph.D.  
November 2, 2001



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